

Patent claims:

1. Biodegradable colloidal particles comprising
  - a) amphiphilic comb polymers comprising a water-soluble polyol backbone, hydrophobic side chains and primary, secondary, tertiary or quaternary side chains carrying amino groups and
  - b) as a stabilizer, at least one negatively charged organic base, which can be a Lewis or Brønsted base, or the corresponding acid thereof, which can be a Lewis or Brønsted acid

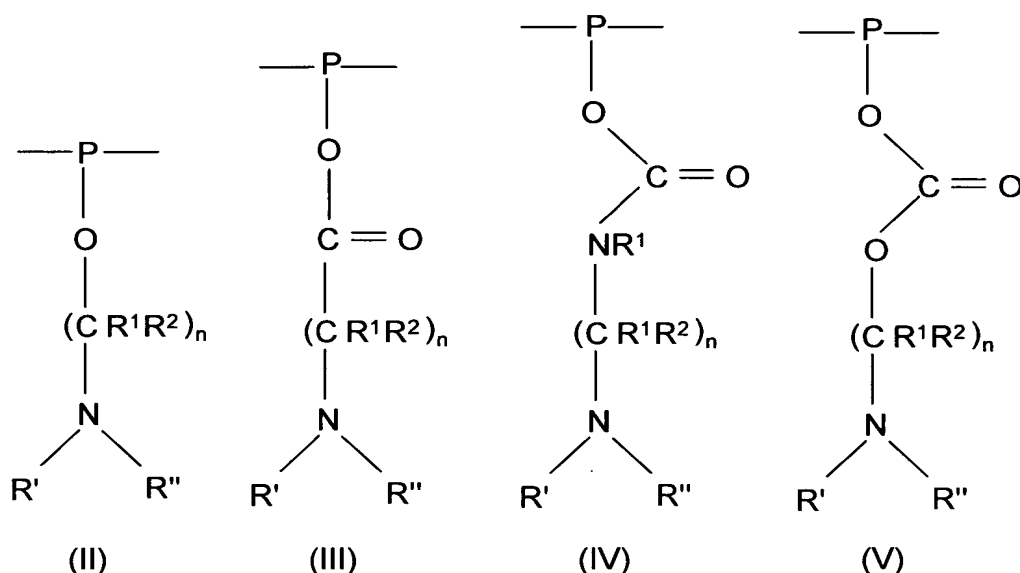
wherein

the acid groups of the stabilizer are available in excess or deficiency in relation to the primary, secondary, or tertiary amino groups of the comb polymers, or

the basic groups are available in deficiency or excess in relation to the quaternary amino groups of the comb polymers,

so that the colloidal particles feature a positive or negative zeta potential.
2. Biodegradable colloidal particles according to claim 1, wherein the organic base or corresponding acid thereof is a pharmaceutically active substance, or a combination comprising several pharmaceutically active substances, or a combination of one or more pharmaceutically active substances and an additive.
3. Biodegradable colloidal particles according to claim 2, wherein the pharmaceutically active substance is a carboxylic acid, sulphonic acid or phosphoric acid.
4. Biodegradable colloidal particles according to claim 3, wherein the active substance is a prostanoid.

5. Biodegradable colloidal particles according to claim 3, wherein the active substance is Iloprost®.
6. Biodegradable colloidal particles according to one of the preceding claims, wherein the side chains carrying amino groups are R groups of the formula [Sg. results from a typo in the German version] (II), (III), (IV), and/or (V),



wherein n represents an integer between 1 and 24 and

P	stands for the polyol backbone and
R', R''	stands [the sg. results from a typo in the German version] independently from one another for H, (C <sub>1</sub> -C <sub>20</sub> )-alkyl, (C <sub>2</sub> -C <sub>10</sub> )-alkenyl, (C <sub>2</sub> -C <sub>10</sub> )-alkinyl, (C <sub>6</sub> -C <sub>22</sub> )-aryl alkyl, wherein the R groups R' and R'' can also be linked to each other and
R <sup>1</sup> , R <sup>2</sup>	stands [the sg. results from a typo in the German version] independently from one another for H, (C <sub>1</sub> -C <sub>10</sub> )-alkyl, (C <sub>2</sub> -C <sub>10</sub> )-alkenyl, (C <sub>2</sub> -C <sub>10</sub> )-alkinyl, (C <sub>5</sub> -C <sub>12</sub> )-aryl, (C <sub>6</sub> -C <sub>22</sub> )-alkyl aryl, (C <sub>6</sub> -C <sub>22</sub> )-aryl alkyl, (C <sub>1</sub> -C <sub>10</sub> )-alkoxy, -O(CO)alkyl-(C <sub>1</sub> -C <sub>10</sub> ), -(CO)O-alkyl-(C <sub>1</sub> -C <sub>10</sub> ), R'R''N-alkyl-(C <sub>1</sub> -C <sub>10</sub> ) or -NR'R'',

wherein also adjacent R groups  $R^1$  or  $R^2$  can be substituted by double or triple bonds, so that a monounsaturated or polyunsaturated carbon chain is available and

wherein up to three  $(CR^1R^2)$  groups can be substituted by an  $-NR^1-$ ,  $=N-$ ,  $-O-$  or  $-(CO)O-$  group, wherein two ether groups or ester groups are not available adjacently and

wherein also at least two of the R groups  $R^1$ ,  $R^2$  can be linked to each other in such a way that a saturated or unsaturated alicyclic, heterocyclic, aromatic or heteroaromatic side chain is available and

wherein the amino groups can be available either completely or partly as quaternary amines of the form  $-(NRR'R'')^+$ , wherein R stands for an H,  $(C_1-C_{20})$ -alkyl,  $(C_2-C_{10})$ -alkenyl,  $(C_2-C_{10})$ -alkinyl or a  $(C_6-C_{22})$ -aryl alkyl R group.

7. Biodegradable colloidal particles according to one of the preceding claims, wherein the comb polymer features a water-soluble polyol backbone chosen from the group of polyalcohols, polyvinyl alcohols, polyvinyl acetates, polysaccharides and dextrans.
8. Biodegradable colloidal particles according to one of the preceding claims, wherein the comb polymer features hydrophobic side chains chosen from the group of polylactides, polyglycolides, poly(lactide-co-glycolides), polytartrates, polycaprolactones, poly(glycolydic-co- $\epsilon$ -caprolactones), poly(lactidic-co- $\epsilon$ -caprolactones), or poly(lactidic-co-glycolidic-co- $\epsilon$ -caprolactones).
9. Biodegradable colloidal particles according to one of the preceding claims, wherein 0.5 to 50 % of the hydroxy groups of the polyol backbone of the comb polymer possess linked side chains carrying amino groups and 1 to 90% of the hydroxy groups of the polyol backbone possess linked hydrophobic side chains.

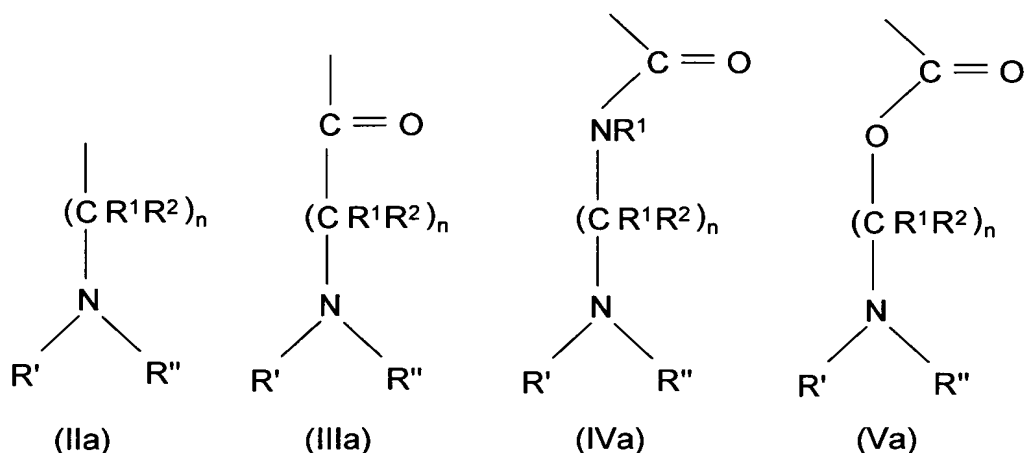
10. Biodegradable colloidal particles according to one of the preceding claims, wherein the amino groups of the comb polymer are at least partly quaternary amino groups, which were quaternized via the addition of an organic acid and stabilized via the corresponding negatively charged organic base which resulted from this.
11. Biodegradable colloidal particles according to one of the preceding claims, wherein the zeta potential lies between -5 and -80 mV or between +5 and +80 mV.
12. Biodegradable colloidal particles according to one of the preceding claims, wherein the organic acid is a prostanoid and the zeta potential lies between -10 and -50 mV or between +10 and +50 mV.
13. Utilization of biodegradable colloidal particles according to one of the claims 1 to 12 for the application of an acidic or basic pharmaceutically active substance for the treatment of diseases in humans and mammals.
14. Utilization of biodegradable colloidal particles according to one of the claims 1 to 12 for the inhalative (pulmonary) application of an acidic or basic active substance.
15. Utilization of biodegradable colloidal particles according to one of the claims 13 or 14, wherein the pharmaceutically active substance is a prostanoid.
16. Utilization of biodegradable colloidal particles according to one of the claims 13 to 15 for the treatment of pulmonary hypertension.
17. Utilization according to one of the claims 13 through 16, wherein the biodegradable colloidal particles are available in a physiologically compatible aqueous solution.

- a) dissolution of a comb polymer comprising a water-soluble polyol backbone, hydrophobic side chains and side chains carrying primary, secondary, tertiary or quaternary amino groups in a water-miscible, volatile organic solvent and
- b) addition of the solution obtained in a) to an isotonic aqueous solution with a pH value between 6.0 and 8.0 comprising, along with a sugar and a buffer, an organic acid, which can be a Lewis or Brønsted acid, or the corresponding base thereof, which can be a Lewis or Brønsted base,
- c) stirring of the solution obtained in (b) for the production of colloidal particles and
- d) removal of the organic solvent.

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P represents a polyol backbone,  
 $R_N$  stands for a side chain carrying amino groups according to the formulas (IIa), (IIIa), (IVa) and/or (Va),



and

$R_x$ ,  $R_y$  and  $R_z$  stands [the sg. results from a typo in the German version] for each of these R groups individually and for each monomer independently from one another for a group chosen from H, (C<sub>1</sub>-C<sub>10</sub>)-alkyl, (C<sub>5</sub>-C<sub>12</sub>)-aryl, (C<sub>6</sub>-C<sub>22</sub>)-alkyl aryl and (C<sub>6</sub>-C<sub>22</sub>)-aryl alkyl and wherein  $R_x$  can also represent a  $-(CO)NR'R''$  group and wherein  $R_y$  and  $R_z$  can also represent a hydroxyl, (C<sub>1</sub>-C<sub>10</sub>)-alkoxy, carboxy, an OCO alkyl-(C<sub>1</sub>-C<sub>10</sub>) or an O(CO)O alkyl-(C<sub>1</sub>-C<sub>10</sub>) group and wherein

i and j stands [the sg. results from a typo in the German version] independently from one another for an integer between 1 and 10 and wherein

m can be an integer between 1 and 100

and wherein

$R^1$ ,  $R^2$ ,  $R'$ ,  $R''$  possess the meaning mentioned in claim 6.

and wherein

the amino groups can be available either completely or partly as quaternary amines of the form  $-(NRR'R'')^+$ , wherein R stands for an H, (C<sub>1</sub>-C<sub>20</sub>)-alkyl, (C<sub>2</sub>-C<sub>10</sub>)-alkenyl, (C<sub>2</sub>-C<sub>10</sub>)-alkinyl or a (C<sub>6</sub>-C<sub>22</sub>)-aryl alkyl R group,

and wherein , relating to the number of the hydroxy functions  $n_{OH}$  of the free polyol backbone

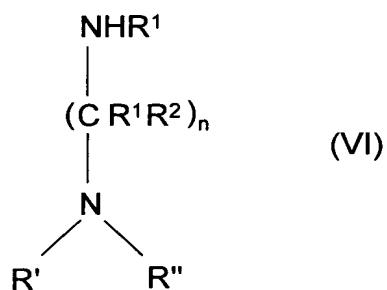
- a is chosen in such a way that the side chains carrying amino groups possess a percentage of 0.5% to 50%
- b is chosen in such a way that the hydrophobic side chains possess a percentage of 1% to 90% and
- c, d can be chosen independently from one another in such a way that the ether side chains and ester side chains possess a percentage between 0% and 98.5%, wherein the percentage of these side chains together is less than  $n_{OH} - (a+b) \%$ .

20. Comb polymer according to claim 19, wherein

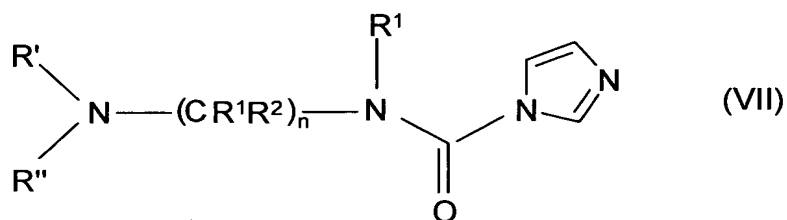
- a is chosen in such a way that the side chains carrying amino groups possess a percentage of 2 % to 35 % and
- b is chosen in such a way that the hydrophobic side chains possess a percentage of 40 % to 70 %.

21. Comb polymer according to either claim 19 or 20, wherein the hydrophobic side chains are chosen from polylactide, polyglycolide, poly(lactide-co-glycolide), polytartrate, polycaprolactone, poly(lactidic-co- $\epsilon$ -caprolactone), poly(glycolydic-co- $\epsilon$ -caprolactone), or poly(lactidic-co-glycolidic-co- $\epsilon$ -caprolactone) R groups.

22. Method for the modification of comb polymers with a polyol backbone with side chains of the formula (IV) according to claim 6, wherein a diamine of the formula (VI),



wherein the R groups R', R'', R<sup>1</sup>, R<sup>2</sup> have the meaning stipulated in claim 6,  
 is reacted with carbonyldiimidazole, and the resulting carbonylimidazole amine (formula (VII))



is linked to a free hydroxy group of the polyol backbone in the presence of an aminopyridine under formation of a urethane linkage.

23. Utilization of comb polymers according to either claim 19 or 20 for the production of biodegradable colloidal particles according to the claims 1 to 12.